

## PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

GARRETT-WACKOWSKI, Eugenia  
Townsend and Townsend and Crew LLP  
Two Embarcadero Center, 8th Floor  
San Francisco, CA 94111-3834  
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 18 April 2001 (18.04.01)	<b>IMPORTANT NOTIFICATION</b>
Applicant's or agent's file reference OPTI004/02WO	
International application No. PCT/US99/26738	International filing date (day/month/year) 12 November 1999 (12.11.99)

## 1. The following indications appeared on record concerning:

☐ the applicant      ☐ the inventor      ☒ the agent      ☐ the common representative

## Name and Address

 EBERLE, Shelley, P.  
Cooley Godward LLP  
3000 El Camino Real  
Five Palo Alto Square  
Palo Alto, CA 94306-2155  
United States of America

## State of Nationality

## State of Residence

## Telephone No.

(650) 843 5000

## Facsimile No.

(650) 857 0663

## Teleprinter No.

## 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☒ the person      ☒ the name      ☒ the address      ☐ the nationality      ☐ the residence

## Name and Address

 GARRETT-WACKOWSKI, Eugenia  
Townsend and Townsend and Crew LLP  
Two Embarcadero Center, 8th Floor  
San Francisco, CA 94111-3834  
United States of America

## State of Nationality

## State of Residence

## Telephone No.

415 576-0200

## Facsimile No.

415 576-0300

## Teleprinter No.

## 3. Further observations, if necessary:

## 4. A copy of this notification has been sent to:

☒ the receiving Office      ☐ the designated Offices concerned  
☐ the International Searching Authority      ☒ the elected Offices concerned  
☒ the International Preliminary Examining Authority      ☐ other:

 The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Maria Victoria CORTIELLO

Telephone No.: (41-22) 338.83.38

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

## PCT

### NOTIFICATION OF RECEIPT OF DEMAND BY COMPETENT INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

(PCT Rule 593(e) and 61.1(b), first sentence  
and Administrative Instructions, Section 601(a))

To:

SHELLEY P. EBERLE  
COOLEY GODWARD LLP  
3000 EL CAMINO REAL  
FIVE PALO ALTO SQUARE  
PALO ALTO CA 94306-2155

Date of mailing  
(day/month/year)

**11 JUL 2000**

Applicant's or agent's file reference  
OPT1004/02W0

#### IMPORTANT NOTIFICATION

International application No.  
PCT/US99/26738

International filing date (day/month/year)  
12 NOV 99

Priority date (day/month/year)  
13 NOV 98

Applicant

OPTIME THERAPEUTICS, INC.

1. The applicant is hereby notified that this International Preliminary Examining Authority considers the following date as the date of receipt of the demand for international preliminary examination of the international application:

30 may 2000

2. That date of receipt is:

- ☒ the actual date of receipt of the demand by this Authority (Rule 61.1(b)).
- ☐ the actual date of receipt of the demand on behalf of this Authority (Rule 59.3(e)).
- ☐ the date on which this Authority has, in response to the invitation to correct defects in the demand (Form PCT/IPEA/404), received the required corrections.

3. ☐ **ATTENTION:** That date of receipt is **AFTER** the expiration of 19 months from the priority date. Consequently, the election(s) made in the demand does (do) not have the effect of postponing the entry into the national phase until 30 months from the priority date (or later in some Offices) (Article 39(1)). Therefore, the acts for entry into the national phase must be performed within 20 months from the priority date (or later in some Offices) (Article 22). For details, see the *PCT Applicant's Guide*, Volume II.

- ☐ (If applicable) This notification confirms the information given by telephone, facsimile transmission or in person on:

4. Only where paragraph 3 applies, a copy of this notification has been sent to the International Bureau.

Name and mailing address of the IPEA/US  
Assistant Commissioner for Patents  
Box PCT  
Washington, D.C. 20231  
Facsimile No.

Attn: IPEA/US

Authorized officer

*D. Russell for Angela Smith*

Telephone No. *703 305-3741*

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: SHELLEY P. EBERLE  
COOLEY GODWARD LLP  
3000 EL CAMINO REAL  
FIVE PALO ALTO SQUARE  
PALO ALTO, CALIFORNIA 94306-2155

## PCT

### NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing  
(day/month/year)

**12 DEC 2000**

Applicant's or agent's file reference

OPTI004/02WO

#### IMPORTANT NOTIFICATION

International application No.

PCT/US99/26738

International filing date (day/month/year)

12 NOVEMBER 1999

Priority Date (day/month/year)

13 NOVEMBER 1998

Applicant

OPTIME THERAPEUTICS, INC.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US

Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

DWAYNE HANDY

Telephone No. (703) 308-0661

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: SHELLEY P. EBERLE  
COOLEY GODWARD LLP  
3000 EL CAMINO REAL  
FIVE PALO ALTO SQUARE  
PALO ALTO, CALIFORNIA 94306-2155

## PCT

### NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Date of Mailing  
(day/month/year)

15 FEB 2000

Applicant's or agent's file reference  
OPTI004/02WO

FOR FURTHER ACTION See paragraphs 1 and 4 below

International application No.  
PCT/US99/26738

International filing date  
(day/month/year)  
12 NOVEMBER 1999

Applicant  
OPTIME THERAPEUTICS, INC.

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland  
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

for  
DWAYNE K. HANDY

Telephone No. (703) 308-0661

SEARCH COPY

# PCT REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For Receiving Office use only

<b>PCT/US 99/26738</b>	
International Application No.	<b>12 NOV 1999</b>
International Filing Date	<b>12.11.99</b>
Name of receiving Office and its full name in the "Application"	
Applicant's or agent's file reference (if desired) (12 characters maximum)	
<b>OPTI004/02WO</b>	

<b>Box No. I</b>	<b>TITLE OF INVENTION</b>	
	<b>METHOD AND APPARATUS FOR LIPOSOME PRODUCTION</b>	
<b>Box No. II</b>	<b>APPLICANT</b>	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e., country) of residence if no State of residence is indicated below.) <b>OPTIME THERAPEUTICS, INC.</b> <b>1333 North McDowell Blvd</b> <b>Petaluma, California 94954-1158</b> <b>United States of America</b>		<input type="checkbox"/> This person is also inventor.  Telephone No. (707) 782-9066  Facsimile No. (707) 782-9096  Teleprinter No.
State (i.e., country) of nationality: US		State (i.e., country) of residence: US
This person is applicant for the purpose of: <input checked="" type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box		
<b>Box No. III</b>	<b>FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTORS</b>	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e., country) of residence if no State of residence is indicated below.) <b>BAKER, Martin T.</b> <b>509 Maria Drive</b> <b>Petaluma, California 94954-1158</b> <b>United States of America</b>		This person is: <input type="checkbox"/> applicant only <input type="checkbox"/> applicant and inventor <input checked="" type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)
State (i.e., country) of nationality:		State (i.e., country) of residence:
This person is applicant for the purpose of: <input type="checkbox"/> All designated States <input type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box		
<input checked="" type="checkbox"/> Further applicants and/or (further) inventors are indicated on a continuation sheet.		
<b>Box No. IV</b>	<b>AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE</b>	
The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: <input checked="" type="checkbox"/> agent <input type="checkbox"/> common representative		
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) <b>EBERLE, Shelley P.</b> <b>COOLEY GODWARD LLP</b> <b>3000 El Camino Real</b> <b>Five Palo Alto Square</b> <b>Palo Alto, California 94306-2155</b> <b>United States of America</b>		Telephone No. (650) 843-5000  Facsimile No. (650) 857-0663  Teleprinter No.
<input type="checkbox"/> Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.		

Form PCT/RO/101 (first sheet) (January 1997; reprint January 1998)

See Notes to the request form

Sheet No. 2

**Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS***If none of the following sub-boxes is used, this sheet is not to be included in the request.*

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e., country) of residence if no State of residence is indicated below.)

**HERIOT, William A.**  
**611 Sunset Cliff Circle**  
**Las Vegas, Nevada 89123**  
**United States of America**

This person is:

- ☐ applicant only
- ☐ applicant and inventor
- ☒ inventor only (If this check-box is marked, do not fill in below.)

State (i.e., country) of nationality:

State (i.e., country) of residence:

This person is applicant for the purpose of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e., country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only (If this check-box is marked, do not fill in below.)

State (i.e., country) of nationality:

State (i.e., country) of residence:

This person is applicant for the purpose of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e., country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only (If this check-box is marked, do not fill in below.)

State (i.e., country) of nationality:

State (i.e., country) of residence:

This person is applicant for the purpose of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e., country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only (If this check-box is marked, do not fill in below.)

State (i.e., country) of nationality:

State (i.e., country) of residence:

This person is applicant for the purpose of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on another continuation sheet.

Form PCT/RO/101 (continuation sheet) (January 1997; reprint January 1998)

See Notes to the request form

**Box No. V DESIGNATION OF STATES**

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

**Regional Patent**

- ☐ **AP ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SZ Swaziland, UG Uganda ZW Zimbabwe and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☐ **EA Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT.
- ☒ **EP European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☐ **OA OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)

**National Patent (if other kind of protection or treatment desired, specify on dotted line):**

- |  |   |
|--|---|
| <input type="checkbox"/> AL Albania.....                               | <input type="checkbox"/> LS Lesotho                                   |
| <input type="checkbox"/> AM Armenia.....                               | <input type="checkbox"/> LT Lithuania                                 |
| <input type="checkbox"/> AT Austria.....                               | <input type="checkbox"/> LU Luxembourg.....                           |
| <input checked="" type="checkbox"/> AU Australia.....                  | <input type="checkbox"/> LV Latvia                                    |
| <input type="checkbox"/> AZ Azerbaijan                                 | <input type="checkbox"/> MD Republic of Moldova.....                  |
| <input type="checkbox"/> BA Bosnia and Herzegovina.....                | <input type="checkbox"/> MG Madagascar.....                           |
| <input type="checkbox"/> BB Barbados                                   | <input type="checkbox"/> MK The former Yugoslav Republic of Macedonia |
| <input type="checkbox"/> BG Bulgaria.....                              | <input type="checkbox"/> MN Mongolia                                  |
| <input type="checkbox"/> BR Brazil.....                                | <input type="checkbox"/> MW Malawi.....                               |
| <input type="checkbox"/> BY Belarus                                    | <input checked="" type="checkbox"/> MX Mexico.....                    |
| <input checked="" type="checkbox"/> CA Canada                          | <input type="checkbox"/> NO Norway                                    |
| <input type="checkbox"/> CH and LI Switzerland and Liechtenstein       | <input type="checkbox"/> NZ New Zealand.....                          |
| <input type="checkbox"/> CN China.....                                 | <input type="checkbox"/> PL Poland.....                               |
| <input type="checkbox"/> CU Cuba.....                                  | <input type="checkbox"/> PT Portugal.....                             |
| <input type="checkbox"/> CZ Czech Republic.....                        | <input type="checkbox"/> RO Romania                                   |
| <input type="checkbox"/> CY Cyprus                                     | <input type="checkbox"/> RU Russian Federation.....                   |
| <input type="checkbox"/> DE Germany.....                               | <input type="checkbox"/> SD Sudan                                     |
| <input type="checkbox"/> DK Denmark.....                               | <input type="checkbox"/> SE Sweden                                    |
| <input type="checkbox"/> EE Estonia.....                               | <input type="checkbox"/> SG Singapore                                 |
| <input type="checkbox"/> ES Spain.....                                 | <input type="checkbox"/> SI Slovenia.....                             |
| <input type="checkbox"/> FI Finland.....                               | <input type="checkbox"/> SK Slovakia.....                             |
| <input type="checkbox"/> GB United Kingdom                             | <input type="checkbox"/> SL Sierra Leone                              |
| <input type="checkbox"/> GE Georgia.....                               | <input type="checkbox"/> TJ Tajikistan.....                           |
| <input type="checkbox"/> GH Ghana.....                                 | <input type="checkbox"/> TM Turkmenistan.....                         |
| <input type="checkbox"/> GM Gambia                                     | <input type="checkbox"/> TR Turkey.....                               |
| <input type="checkbox"/> GW Guinea-Bissau.....                         | <input type="checkbox"/> TT Trinidad and Tobago.....                  |
| <input type="checkbox"/> HU Hungary.....                               | <input type="checkbox"/> UA Ukraine.....                              |
| <input type="checkbox"/> ID Indonesia                                  | <input type="checkbox"/> UG Uganda.....                               |
| <input checked="" type="checkbox"/> IL Israel.....                     | <input type="checkbox"/> US United States of America                  |
| <input type="checkbox"/> IS Iceland                                    | <input type="checkbox"/> UZ Uzbekistan.....                           |
| <input checked="" type="checkbox"/> JP Japan.....                      | <input type="checkbox"/> VN Viet Nam.....                             |
| <input type="checkbox"/> KE Kenya.....                                 | <input checked="" type="checkbox"/> YU Yugoslavia.....                |
| <input type="checkbox"/> KG Kyrgyzstan.....                            | <input type="checkbox"/> ZW Zimbabwe.....                             |
| <input type="checkbox"/> KP Democratic People's Republic of Korea..... |   |
| <input type="checkbox"/> KR Republic of Korea.....                     |   |
| <input type="checkbox"/> KZ Kazakhstan.....                            |   |
| <input type="checkbox"/> LC Saint Lucia.....                           |   |
| <input type="checkbox"/> LK Sri Lanka                                  |   |
| <input type="checkbox"/> LR Liberia                                    |   |

Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after Issuance of this sheet:

In addition to the designations made above, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except the designation(s) of \_\_\_\_\_

The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

**Supplemental Box***If the Supplemental Box is not used, this sheet need not be included in the request.**Use this Box in the following cases:***1. If, in any of the Boxes, the space is insufficient to furnish all the information:***in particular:*

- (i) if more than two persons are involved as applicants and/or inventors and no "continuation sheet" is available:
- (ii) if, in Box No. II or in any of the sub-boxes of Box No. III, the indication "the States indicated in the Supplemental Box" is checked:
- (iii) if, in Box No. II or in any of the sub-boxes of Box No. III, the inventor or the inventor/applicant is not inventor for the purposes of all designated States or for the purposes of the United States of America:
- (iv) if, in addition to the agent(s) indicated in Box No. IV, there are further agents:
- (v) if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication "patent of addition," or "certificate of addition," or if, in Box No. V, the name of the United States of America is accompanied by an indication "Continuation" or "Continuation-in-part":
- (vi) if there are more than three earlier applications whose priority is claimed:

*in such case, write "Continuation of Box No...." [indicate the number of the Box] and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient;**in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III;**in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, European or OAPI patent) for the purposes of which the named person is applicant;**in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, European or OAPI patent) for the purposes of which the named person is inventor;**in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV;**in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;**in such case, write "Continuation of Box No. VI" and indicate for each additional earlier application the same type of information as required in Box No. VI.***2. If the applicant claims, in respect of any designated Office, the benefits of provisions of the national law concerning non-prejudicial disclosures or exceptions to lack of novelty:***in such case, write "Statement Concerning Non-Prejudicial Disclosures or Exceptions to Lack of Novelty" and furnish that statement below.***Continuation of Box No. IV**

Baran, Alexandra J.  
 Eberle, Shelley P.  
 Goldman, Richard M.  
 Leal, Peter R.  
 Moran, Tom M.  
 \*\*\*Pade, Jeffrey A.  
 \*\*Richardson, Bryan D.  
 Sachdeva, Gurjeev K.  
 Wallach, Brenda


\* Brodsky, Aaron S.  
 Ewing, Thomas L.  
 Higgins, Willis E.  
 Lillis, Marcella  
 Neeley, Richard L.  
 Postner, Marya A.  
 \*\*\*Richman, Howard R.  
 \*\*\*Talbot, Scott C.  
 Yim, Peter J.

de Villiers, P. Francois  
 Flick, Karen E.  
 \*\*\*Kobayashi, Duane S.  
 \*\*\*Lynch, Thomas W.  
 Opperman, Craig P.  
 Rhyu, Michelle S.  
 Ropp, Traci H.  
 \*\*\*Rick A. Toering  
 \*\* Zimmer, Kevin J.

**The above attorneys and agents are members of the law firm of Cooley Godward LLP. The address is the same as that shown in Box No. IV.****\* The address is 2595 Canyon Boulevard, Suite 250, Boulder, Colorado 80302-6737, U.S.****\*\* The address is 4365 Executive Drive, Suite 1100, San Diego, California 92121-2128, U.S.****\*\*\*The address is 2002 Edmund Halley Drive, Suite 300, Reston, Virginia 20191, U.S.****In addition to the countries designated, applicant hereby designates any country not listed, but that is a contracting member of the Patent Cooperation Treaty at the time of filing.**



Sheet No. 5

<b>Box No. VI PRIORITY CLAIM</b>		Further priority claims are indicated in the Supplemental Box <input type="checkbox"/>	
The priority of the following earlier application(s) is hereby claimed:			
Country (in which, or for which, the application was filed)	Filing Date (day/month/year)	Application No.	Office of filing (only for regional or international application)
Item (1) US	13 November 1998 (13.11.98)	60/108,355	
Item (2)			
Item (3)			
Mark the following check-box if the certified copy of the earlier application is to be issued by the Office for which the purposes of the present international application is the receiving Office (a fee may be required):			
<input type="checkbox"/> The receiving Office is hereby requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s): (1)			
<b>Box No. VII INTERNATIONAL SEARCHING AUTHORITY</b>			
Choice of International Searching Authority (ISA) (If two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used): <b>ISA/ US</b>			
Earlier search Fill in where a search (international, international-type or other) by the International Searching Authority has already been carried out or requested and the Authority is now requested to base the international search, to the extent possible, on the results of that earlier search. Identify such search or request either by reference to the relevant application (or the translation thereof) or by reference to the search request: Country (or regional Office): _____ Date (day/month/year): _____ Number: _____			
<b>Box No. VIII CHECK LIST</b>			
This international application contains the following number of sheets:		This international application is accompanied by the item(s) marked below:	
1. request : 5 sheets	2. description : 38 sheets	3. Sequence Listings : 0 sheets	4. claims : 7 sheets
5. Appendices (1-3) : 0 sheets	6. Abstract : 1 sheet	7. drawings : 9 sheets	Total : 60 sheets
1. <input type="checkbox"/> Separate signed power of attorney		5. <input checked="" type="checkbox"/> fee calculation sheet	
2. <input type="checkbox"/> copy of general power of attorney		6. <input type="checkbox"/> separate indications concerning deposited microorganisms	
3. <input type="checkbox"/> statement explaining lack of signature		7. <input type="checkbox"/> nucleotide and/or amino acid sequence listing (diskette)	
4. <input type="checkbox"/> priority document(s) identified in Box No. VI as item(s):		8. <input checked="" type="checkbox"/> other (specify): <b>Transmittal PTO-1382, POSTCARD</b>	
Figure No. _____ of the drawings (if any) should accompany the abstract when it is published.			
<b>Box No. IX SIGNATURE OF APPLICANT OR AGENT</b>			
Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request.)			
 Shelley P. Eberle <div style="float: right; margin-top: 10px;">(12-11-99)</div>			
For receiving Office use only			
1. Date of actual receipt of the purported international application:		<b>524 Rec'd PCT/PTO 12 NOV 1999</b>	
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:		2. Drawings: <input type="checkbox"/> received:  <input type="checkbox"/> not received:	
4. Date of timely receipt of the required corrections under PCT Article 11(2):			
5. International Searching Authority specified by the applicant: <b>ISA/US</b>			
6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid.			
For International Bureau use only			
Date of receipt of the record copy by the International Bureau: _____			

Form PCT/RO/101 (last sheet) (January 1994; reprint January 1998)

See Notes to the request form

# PCT

## FEE CALCULATION SHEET

Annex to the Request

PCT/US 99/26738

International Application No.

(12.11.99)

12 NOV 1999

Applicant's or agent's  
file reference:

OPTI004/02WO

Date stamp of the receiving Office

Applicant:

OPTIME THERAPEUTICS, INC.

## CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE ..... 240.00 T
2. SEARCH FEE ..... 700.00 S
- International search to be carried out by US  
(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the international search.)
3. INTERNATIONAL FEE
- Basic Fee**  
The international application contains 60 sheets.  
first 30 sheets ..... 455.00 b  
30 x 10.00 = 300.00 β  
remaining sheets additional amount B
- Add amounts entered at b<sub>1</sub> and b<sub>2</sub> and enter total at B. .... 755.00
- Designation Fee**  
The international application contains 7 designations.  
7 x 105.00 = 735.00 D  
number of designations amount of designation fee  
payable (maximum 10)
- Add amounts entered at B and D and enter total at I. .... 1,490.00 I  
(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the sum of the amounts entered at B and D)
4. FEE FOR PRIORITY DOCUMENT ..... 15.00 P
5. TOTAL FEES PAYABLE \$2,445.00
- Add amounts entered at T, S, I and P,  
and enter total in the TOTAL box TOTAL

☐ The designation fee is not paid at this time.

## MODE OF PAYMENT

- ☐ authorization to charge deposit account (see below) ☐ bank draft ☐ coupons
- ☒ cheque ☐ cash ☐ Other (specify)
- ☐ postal money order ☐ revenue stamps

Deposit Account Authorization (this mode of payment may not be available at all receiving Offices)

- The RO/ US ☐ is hereby authorized to charge the total fees indicated above to my deposit account.
- ☒ is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.
- ☒ is hereby authorized to charge the fee for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account.

03-3117  
Deposit Account Number12/NOV/99  
Date (day/month/year)Shelley P. Eberle  
Signature Shelley P. Eberle

# PCT

## POWER OF ATTORNEY

(for an international application filed under the Patent Cooperation Treaty)

(PCT Rule 90.4)

The undersigned applicant(s) (Names should be indicated as they appear in the request):

**OPTIME THERAPEUTICS, INC.**  
1333 North McDowell Boulevard  
Petaluma California 94954-1158  
United States of America

hereby appoints (appoint) the following person as: ☒ agent(s) ☐ common representative(s)

**Name(s) and address(es)**

(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

Marcella Lillis, Alexandra J. Baran, Shelley P. Eberle, Aaron S. Brodsky\*, Willis E. Higgins,  
Peter R. Leal, Tom M. Moran, Richard L. Neeley, Craig P. Opperman, Gurjeet K. Sachdeva,  
Richard M. Goldman, Kevin J. Zimmer\*\*, Michelle Rhyu, Karen E. Flick, Peter J. Yim, Marya A. Postner,  
Thomas L. Ewing, Duane S. Kobayashi\*\*\*, Bryan D. Richardson\*\*, Howard R. Richman\*\*\*, C. Scott Talbot\*\*\*,  
Rick A. Toering\*\*\*, Jeffrey A. Pade\*\*\*, Traci Ropp, Thomas W. Lynch\*\*\*

All of COOLEY GODWARD LLP, 5 Palo Alto Square, 3000 El Camino Real, Palo Alto, California 94306-2155, U.S.A

\* 2595 Canyon Boulevard, Suite 250, Boulder, Colorado 80302-6737, U.S.A.

\*\* 4365 Executive Drive, Suite 1100, San Diego, California 92121-2128, U.S.A.

\*\*\* 2002 Edmund Halley Drive, Suite 300, Reston, VA 20191 U.S.A.

to represent the undersigned before ☒ all the competent International Authorities  
☐ the International Searching Authority only  
☐ the International Preliminary Examining Authority only

in connection with the international application identified below:

**Title of the invention: METHOD AND APPARATUS FOR LIPOSOME PRODUCTION BACKGROUND OF THE INVENTION**

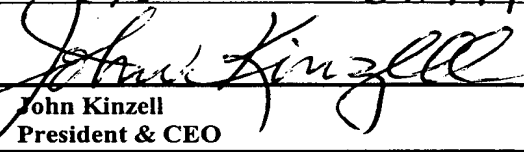
**Applicant's or agent's file reference: OPTI004/02WO**

**International application number (if already available):**

filed with the following Office \_\_\_\_\_ as receiving Office  
and to make to receive payments on behalf of the undersigned.

**Signature of the applicant(s)** (where there are several applicants, each of them must sign; next to each signature, indicate the name of the person signing and the capacity in which the person signs, if such capacity is not obvious from reading the request or this power):

Date:

22 November 1999  
X   
NAME: John Kinzell  
TITLE: President & CEO

Form PCT/Model of power of attorney (for a given international application) (July 1992)

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

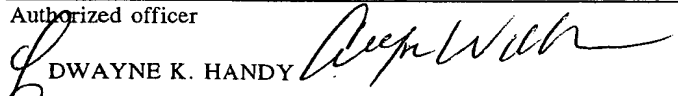
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference OPTI004/02WO	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US99/26738	International filing date (day/month/year) 12 NOVEMBER 1999	Priority date (day/month/year) 13 NOVEMBER 1998
International Patent Classification (IPC) or national classification and IPC IPC(7): B01J 13/02 and US Cl.: 264/4.1 ; 436/829		
Applicant OPTIME THERAPEUTICS, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 3 sheets.
- ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of 0 sheets.

## 3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand  30 MAY 2000	Date of completion of this report  08 NOVEMBER 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer  DWAYNE K. HANDY
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0661

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/26738

**I. Basis of the report**1. With regard to the **elements** of the international application:\*

- ☒ the international application as originally filed
- ☒ the description:  
pages 1-38 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_
- ☒ the claims:  
pages 39-45 , as originally filed  
pages NONE , as amended (together with any statement) under Article 19  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_
- ☒ the drawings:  
pages 1-9 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_
- ☒ the sequence listing part of the description:  
pages NONE , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE
- ☒ the claims, Nos. NONE
- ☒ the drawings, sheets/fig NONE

5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/26738

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

## 1. statement

Novelty (N)

Claims 1-57 YESClaims NONE NO

Inventive Step (IS)

Claims 1-57 YESClaims NONE NO

Industrial Applicability (IA)

Claims 1-57 YESClaims NONE NO

## 2. citations and explanations (Rule 70.7)

Claims 1-57 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest a mixing device as disclosed by applicant in claim 1, part(c). The prior art also fails to suggest a method for the production of lipids which includes the mixing device as recited by applicant in claim 34, part c. The closest prior art (Martin, West III, Yiournas) does not disclose nor suggest an apparatus for the continuous production of lipid vesicles with a mixing device which contains the following elements: a premixing system, a mixer, several metering systems and several transfer means for transferring lipids and other compounds to and from the various elements of the mixing device. The same mixing device elements are also present in the method presented in claim 34.

Claims 1-57 meet the criteria set out in PCT Article 33(4), because the apparatus and method of lipid production have use in drug synthesis and drug delivery.

----- NEW CITATIONS -----

NONE

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference OPTI004/02WO	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US99/26738	International filing date (day/month/year) 12 NOVEMBER 1999	(Earliest) Priority Date (day/month/year) 13 NOVEMBER 1998
Applicant OPTIME THERAPEUTICS, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☐ Certain claims were found unsearchable (See Box I).
2. ☐ Unity of invention is lacking (See Box II).
3. ☐ The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing
  - ☐ filed with the international application.
  - ☐ furnished by the applicant separately from the international application,
    - ☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
  - ☐ transcribed by this Authority.
4. With regard to the title,
  - ☒ the text is approved as submitted by the applicant.
  - ☐ the text has been established by this Authority to read as follows:
5. With regard to the abstract,
  - ☒ the text is approved as submitted by the applicant.
  - ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
6. The figure of the drawings to be published with the abstract is:  
Figure No. \_\_\_\_\_
  - ☐ as suggested by the applicant.
  - ☐ because the applicant failed to suggest a figure.
  - ☐ because this figure better characterizes the invention.

☒ None of the figures.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US99/26738

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(6) :B01J 13/02

US CL :264/4.1 ; 436/829

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 264/4.1, 4.4 ; 436/829; 422/130 ; 424/9.321, 450

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4,781,871 A (WEST, III et al) 01 November 1988, Figures 1 and 3, column 5, lines 22-30, column 6, lines 25-58, columns 12-13.	1 , 2 , 5 - 8,14,16,18,21,2 2 , 26 - 28 , 34 , 35,38,46,47,50,5 1,54,56
Y	US 4,752,425 A (MARTIN et al) 21 June 1988, Figures 1 and 3, column 5, lines 22-30, column 6, lines 25-58, columns 12 and 13.	1 , 2 , 5 - 8,14,16,18,21,2 2 , 26 - 28,34,35,38,46,4 7,50,51,54,56
Y	US 4,895,452 A (YIOURNAS et al) 23 January 1990, Figure 3, column 1, lines 65-68, columns 6 and 7.	1 , 2 , 6 , 11 , 1 4 , 18 , 26 , 27 , 34,35,43

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A" document defining the general state of the art which is not considered to be of particular relevance	*X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*E" earlier document published on or after the international filing date	*Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*&"	document member of the same patent family
*O" document referring to an oral disclosure, use, exhibition or other means		
*P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 03 FEBRUARY 2000	Date of mailing of the international search report 15 FEB 2000
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer <i>John P. Hardy</i> DWAYNE K. HANDY Telephone No. (703) 308-0661



## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/26738

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,013,497 A (YIOURNAS et al) 07 May 1991, Figure 3, column 2, lines 1-5, columns 6 and 7.	1,2,6,11,14 ,18,26,27,3 4,35,43
Y	US 5,700,482 A (FREDERIKSEN et al) 23 December 1997, column 8, lines 35-65, column 9, lines 1-35, column 10, lines 20-55.	1,3,5,16,17,22,26, 28,30,32,34,36,38, 46,50,5 2,56
Y	US 4,551,288 A (KELLY) 05 November 1985, column 2, lines 40-59, column 4, lines 35-60.	1,34,41
Y	US 5,554,382 A (CASTOR) 10 September 1996, column 4, lines 25-52, columns 6-7.	1,2,4-8,14,26- 28,30,32,34,35,37, 38,50-52
Y	US 5,271,881 A (REDDING, JR.) 21 December 1993, column 24, example 1.	12, 44
A	US 5,453,447 A (END et al) 26 September 1995, entire document.	
A	US 5,558,820 A (NAGANO et al) 24 September 1996, entire document.	
A	US 4,935,171 A (BRACKEN) 19 June 1990, entire document.	

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US99/26738

## B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

EAST database

search terms: mixer, inline mixer, static mixer, liposome, lipid vesicle, multilamellar, oligolamellar, sonication, ivermectin, diclofenac